REMARKS

Upon entry of the present amendment, claims 7 will be amended, and claims 12, 14, 23, 24, and 27 will be canceled, whereby claims 7-11, 13, 16-22, 25, and 26 will be pending.

The amendment to claim 7 incorporates elements from claims 12 and 14. Thus, support for the amendments is found, at least, in prior claims 12 and 14.

Applicants request reconsideration of the rejection and allowance of the application in view of the following remarks.

Response to Art Based Rejections

The Action rejects claims 7, 9, 11-14, 16, 20, 22, 24 and 26 under 35 U.S.C. 102(b) as being anticipated by U.S. Patent No. 5,891,192 to Murayama et al. In response, Applicants respectfully submit that Murayama et al. does not anticipate the presently claimed invention.

Applicants respectfully submit that this ground of rejection is without appropriate basis because Murayama et al. does not first treat the silicone prior to application of the protein. For ease of reference, Applicants note that claim 7 recites, among other elements, "irradiating at least a portion of a surface of the expanded polytetra-fluoroethylene or silicone with ions at a dose (φ) of $1 \times 10^{12} \leq \varphi \leq 1 \times 10^{16}$ ions/cm^2 to form an ion-modified expanded polytetra-fluoroethylene or silicone; and applying the fibrin glue to the irradiated at least a portion of a surface of the expanded polytetra-fluoroethylene or silicone." In contrast, Murayama et al. first applies the protein to the implant and then the coated implant is subjected to ion implantation.

Applicants respectfully submit that Murayama et al. fails to disclose at least this aspect of the claimed invention, and thus, the rejection is improper and should be withdrawn.

The Action rejects claims 7-14, 17, 19, 21, 23, 25 and 27 under 35 U.S.C. 103(a) as being unpatentable over Whitmore et al., U.S. Patent No. 6,503,527, in view of Suzuki et al., Ionics, Vol. 25, No. 1, pp. 47-54.

In response to this ground of rejection, Applicants once again note their arguments as previously submitted with the previous responses, and incorporate these arguments as if set forth in their entirety herein. For the Examiner's convenience in having arguments appearing in one location for review, Applicants are repeating previously presented arguments while modifying these arguments with respect to the claims as amended herein.

Applicants again submit that Whitmore et al. relates to a substance that is obtained by chemically immobilizing fibrin-constituting component, such as fibrinogen to hyaluronic acid, chitin, or chitosan. Whitmore et al. discloses hyaluronic acid, hyaluronic acid derivative, chitin, chitosan, or its derivatives, having an adhesive property with a fibrin glue, and its structure product. Hyaluronic acid, chitin, and chitosan are biologically derived materials. In contrast, the presently claimed subject matter relates to, as recited in Applicants' independent claim 7, a method for improving affinity with a fibrin glue of a polymeric material comprising carbon or silicon as a constitutional element, the polymeric material comprising expanded polytetra-fluoroethylene or silicone, comprising irradiating at least a portion of a surface of the expanded polytetra-fluoroethylene or silicone with ions at a dose (φ) of $1 \times 10^{12} \leq \varphi \leq 1 \times 10^{16}$ ions/cm^2 to form an ion-modified expanded

polytetra-fluoroethylene or silicone; and applying the fibrin glue to the irradiated at least a portion of a surface of the expanded polytetra-fluoroethylene or silicone, wherein the ion is He^+, Ne^+, Ar^+, or Kr^+.

Thus, in Applicants' recited method, the fibrin glue is applied to the irradiated at least a portion of the irradiated expanded polytetra-fluoroethylene or silicone to improve affinity of the expanded polytetra-fluoroethylene or silicone. At most, Whitmore et al. discloses the broad anchoring of dural patches. Applicants submit that it is a generally known fact that fibrin glue usually can be used in surgery for repair of dura mater. Whitmore et al. is therefore, at best, only directed to a conventional surgery method in which a fibrin glue is used for prevention of a leak of cerebrospinal fluid in dura mater surgery. Whitmore et al. does not teach or suggest expanded polytetra-fluoroethylene or silicone to which fibrin glue is adhered being formed by irradiation as recited in Applicants' claims.

Applicants also note that Whitmore et al. discloses, beginning at column 2, line 45, that his invention relates to a fibrin glue composition comprised of a biocompatible, bioabsorbable hyaluronic acid derivative material, having applied thereto fibrinogen and thrombin. Beginning at column 2, line 62, Whitmore et al. discloses that when placed on a wound site and activated, the compositions of his invention function as a fibrin glue, and that in contrast to conventional fibrin glues, his compositions do not require complex mixing of fibrinogen and thrombin components immediately prior to use and further, do not require special applicators.

Thus, Whitmore et al. is directed to a fibrin adhesive or sealant composition comprising a biocompatible, bioabsorbable hyaluronic acid material, chitin material, or chitosan material to which fibrogen and a fibrinogen cleaving agent are applied along

with other components. Applicants submit that one having ordinary skill in the art would not have been motivated to use the disclosed film, or woven or non-woven material of Whitmore et al., with an ion-bombarded polymeric material as recited in Applicants' claims.

Whitmore et al. also discloses uses of his compositions at the top of column 3, including a wide range of suitable medical and surgical uses, and he notes that the compositions can be used in hemostasis applications, as sealants and as adhesives. Moreover, it Whitmore et al. discloses that the compositions of his invention have a number of surgical uses, including, in cardiovascular surgery, they can be used as a hemostatic, for example, with needle holes, suture lines, diffuse and nonspecific bleeding, friable tissue bleeding, aortic dissections, ventricular ruptures, and fistulas. In otorhinolaryngology (ear, nose and throat, ENT) surgery, it is disclosed that they can be used in facial nerve grafts, closure of dural leaks, nasal septal surgeries, and post tonsillectomy hemorrhage. In neurosurgery, he discloses that they can be used to prevent cerebral spinal fluid (CSF) leakage, peripheral nerve repair, and to anchor dural patches. In plastic surgery, it is disclosed that they can be used in a number of procedures relating to skin grafts, including to fix grafts, control oozing, and control bleeding. In thoracic surgery, they can be used, for example, in the treatment of pneumothorax and pulmonary leaks. The compounds of Whitmore et al.'s invention are also disclosed to have a number of other surgical uses, including, sealing biopsy needle tracks, liver and splenic lacerations, lymphatic fluid leaks, organ resectioning, seroma and hematoma prevention, and gastrointestinal bleeding. Whitmore et al. also discloses that his compositions can be used as a local delivery vehicle for the delivery antibiotics or other biologically active substances to the application site. Whitmore et al. also discloses that his compositions

may serve as a surgical adhesion barrier, and that other uses are known in the art or will be apparent to the skilled artisan.

Thus, as the rejection realizes, amongst a multitude of uses, Whitmore et al. broadly discloses use of a dural patch, but does not disclose a dural patch as recited in Applicants' claims. In this regard, as noted above, Applicants' independent claim 7 is directed to a method for improving affinity with a fibrin glue of a polymeric material comprising carbon or silicon as a constitutional element, the polymeric material comprising expanded polytetra-fluoroethylene or silicone, comprising irradiating at least a portion of a surface of the expanded polytetra-fluoroethylene or silicone with ions at a dose (φ) of $1 \times 10^{12} \leq \varphi \leq 1 \times 10^{16}$ ions/cm^2 to form an ion-modified expanded polytetra-fluoroethylene or silicone; and applying the fibrin glue to the irradiated at least a portion of a surface of the expanded polytetra-fluoroethylene or silicone, wherein the ion is He^+, Ne^+, Ar^+, or Kr^+.

In an attempt to overcome this deficiency of Whitmore et al., the rejection relies upon Suzuki et al. (which includes as an author, Yoshiaki Suzuki, who is one of the inventors of the presently claimed subject matter). However, one having ordinary skill in the art would not have combined these diverse disclosures. Suzuki et al. discloses that cells are adhered to a polymer that was irradiated with an ion beam, and its adhesion strength is improved by irradiation of the ion beam. As disclosed, in Suzuki et al., such as beginning at page 7, 2.3 Cell culturing method, the cells are cultured *in vitro*, and the cells are selectively adhered to the polymer which was irradiated with the ion beam. In such an "*in vitro*" experiment of cell culturing, the culture solution that contains cells does not contain fibrogen. The culture solution contains amino acid and serum, which is plasma from which fibrinogen is removed. From the results of the *in vitro* experiment of Suzuki et al., one having ordinary skill in the art would not be capable of predicting that fibrinogen, which is

one component of fibrin glue, is adsorbed to a polymer which was irradiated with an ion beam.

Applicants note that the main component of serum is albumin (45%). Based upon the disclosures, even if for the sake of argument the documents were combined, adsorption of albumin may be predicted, but adsorption of fibrinogen would not be predicted. In this regard, prediction based upon an experiment in the absence of fibrinogen is without any support as to any expectation of results with fibrinogen.

Thus, Suzuki et al. discloses that cells are adhered to a polymer that was irradiated with an ion beam, and adhesion strength of the polymer is improved by irradiation of ion beam. However, Suzuki et al. does not teach that the adsorption of fibrinogen, which is a plasma protein, is increased. One having ordinary skill in the art would not be able to predict that the adsorption of fibrinogen is increased in the case of using ion beam-irradiated ePTFE. If it is predicted from Suzuki et al. that the adsorption of fibrinogen is increased by irradiating ePTFE with ion beam, then the adsorption amount of all proteins would be increased. However, this is not a fact. In the cell culturing of Suzuki et al., the culture solution contains a serum (from which fibrinogen was removed). Therefore, it may be considered that adsorption amount of fibronectin or vitronectin, which is involved in cell adhesion, is increased, but the adsorption amount of proteins, which are not present therein, cannot be predicted. The proteins include both proteins that promote cell adhesion and proteins that inhibit cell adhesion. Thus, there is the possibility that the adsorption amount of proteins that inhibit cell adhesion will be increased.

Still further, the Examiner is reminded that independent claim 7 is directed to a method for improving affinity with a fibrin glue of a polymeric material comprising carbon or silicon as a constitutional element, the polymeric material comprising expanded

polytetra-fluoroethylene or silicone, comprising irradiating at least a portion of a surface of the expanded polytetra-fluoroethylene or silicone with ions at a dose (φ) of $1 \times 10^{12} \leq \varphi \leq 1 \times 10^{16}$ ions/cm^2 to form an ion-modified expanded polytetra-fluoroethylene or silicone; and applying the fibrin glue to the irradiated at least a portion of a surface of the expanded polytetra-fluoroethylene or silicone, wherein the ion is He^+, Ne^+, Ar^+, or Kr^+. This is different from repairing a body tissue by using an ion beam-irradiated polymeric material. A review of Applicants' originally filed application, including the Examples reveals that it is unexpected that the adhesiveness between ePTFE and a fibrin glue was remarkably improved in the case of ion beam-irradiated ePTFE as compared with the case of untreated ePTFE (Figs 1 and 2).

Still further, Applicants once again note that a copy of Kobayashi et al., Surface & Coatings Technology 201 (2007) 8039-8042 was submitted April 22, 2009. A review of this document should reveal that it is unexpected that the adhesiveness between silicone sheets and a fibrin glue is remarkably improved in the case of ion beam-irradiated silicone sheets as compared with untreated silicone sheets. For example, attention is once again directed to Kobayashi et al., page 8042, Fig. 7 and its discussion in the paragraph beginning at the bottom of the right-hand column.

Additionally, Applicants present two additional publications.[1] Takahashi et al., *Transactions of the Materials Research Society of Japan* **29**[2]: 591-594 (2004), and Takahashi et al., *Neurological Surgery* **31**(10): 1081-1088 (2003) (which is written in Japanese, but includes an English language abstract) as further evidence of the

[1] In accordance with MPEP 609, these documents are being submitted in support of Applicants' arguments, and without being listed on a Form PTO-1449. Accordingly, a fee should not be necessary for their consideration. However, authorization is hereby provided to charge any required fee to Deposit Account No. 19-0089.

nonobviousness of the present invention. While Applicants invite the Examiner to review these publications in full and weigh their impact on the outstanding rejections, Applicants do wish to point out that both describe expanded polytetrafluoroethylene irradiated with He^+, Ne^+, Ar^+, or Kr^+ at doses of $1x10^{14}$, $5x10^{14}$, and $1x10^{15}$ ions/cm^2. Applicants submit that the results shown in the publications should be considered commensurate in scope with the present claims.

Finally, with respect to the Office's suggestion that evidence of unexpected results *must* be in affidavit or declaration form, Applicants respectfully disagree. The Office is required to consider all evidence when weighing the nonobviousness of a claimed invention, and is not free to ignore evidence disclosed in Applicants' own publications simply because it is not presented in affidavit or declaration form. As noted in MPEP 716.02(g), cited by the Office, "[p]ublications may . . . be evidence of the facts in issue and should be considered to the extent that they are probative." Applicants respectfully submit that the unexpected results shown in the above-referenced publications are especially probative of the nonobviousness of the present invention.

For the reasons set forth above, the advantageous effect of the present invention cannot be predicted from Whitmore et al. and Suzuki et al.

Accordingly, Applicants submit that the one having ordinary skill in the art would not have arrived at the subject matter recited in Applicants' claims and/or the results as disclosed and claimed by Applicants. Moreover, Applicants again submit that the results shown herein should be considered to be commensurate with the claimed subject matter.

The Action further rejects claims 16, 18, 20, 22, 24 and 26 under 35 U.S.C. 103(a) as being unpatentable over Whitmore et al., U.S. Patent No. 6,503,527, in view of Suzuki

et al., Ionics, Vol. 25, No. 1, pp. 47-54, and further in view of US 2004/0005364 to Klein et al.

For the reasons set forth above, Applicants respectfully submit that Whitmore et al. in view of Suzuki et al. fails to establish the obviousness of, at least, claim 7. Applicants respectfully note that Klein et al. fails to satisfy any deficiencies with respect to Whitmore et al. or Suzuki et al., as applied to claim 7. As claims 16, 18, 20, 22, and 26 depend ultimately from claim 7, they are patentable over the cited art for the same reasons as claim 7 is patentable over the cited art. Applicants note that claim 24 is canceled.

Thus, Applicants respectfully request the withdrawal of the rejection for obviousness over Whitmore et al., U.S. Patent No. 6,503,527, in view of Suzuki et al., Ionics, Vol. 25, No. 1, pp. 47-54, and further in view of US 2004/0005364 to Klein et al.

Based on all of the foregoing remarks and amendments, Applicants respectfully submit that this application is in condition for allowance, the rejection should be withdrawn, and respectfully request the mailing of a Notice of Allowance.

CONCLUSION

In view of the foregoing, the Examiner is respectfully requested to reconsider and withdraw the objection and rejections of record, and allow each of the pending claims.

Applicants therefore respectfully request that an early indication of allowance of the application be indicated by the mailing of the Notices of Allowance and Allowability.

Should the Examiner have any questions regarding this application, the Examiner is invited to contact the undersigned at the below-listed telephone number.

Respectfully submitted,
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Attachments:

- Takahashi et al., *Transactions of the Materials Research Society of Japan* **29**[2]: 591-594 (2004)
- Takahashi et al., *Neurological Surgery* **31**(10): 1081-1088 (2003)

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